

EQUIPMENT - CHODERA LABORATORY

Experimental.

Gravimetric solution preparation: Biophysical measurements of protein-ligand binding affinities are fundamentally limited by the accuracy with which compound concentrations are known. Accurate affinity measurements are absolutely essential to validating and improving computational methodologies for probing and predicting binding affinities, so it is essential that compound concentrations be known precisely and accurately. Methods to *measure* concentrations are generally costly, inaccurate, time-consuming, and often not universally applicable. Precise preparation of initial compound solutions remains the best way to ensure accuracy. Our laboratory is therefore equipped with a high-precision Mettler-Toledo Quantos balance for automated gravimetric solution preparation. Powder dosing heads dose compound directly into solubilization vials on the analytical balance, while liquid dosing heads dispense solvent under argon, ensuring accurate concentrations of compound solutions. Provenance, masses, concentrations, and uncertainties are tracked via barcodes and electronically within our ELN.

Integrated liquid handler and automation platform: By the start of this award, the experimental laboratory will be equipped with a high-throughput automation platform for 96- and 384-well biophysical assays. The automated system will integrate the following instruments: a high-precision liquid-handling platform equipped for vacuum filtration, density measurement, and thermal cooling/heating/shaking; a high-end multimode plate reader with injectors; heating/shaking deep well plate incubators for bacterial culture; a plate centrifuge; a qPCR machine used for PCR and ThermoFluor; a microplate sealer; barcode-based tracking capabilities; an automated plate carousel; and a microfluidic gel electrophoresis system. A LabMinds EasySolution automated buffer preparation system will ensure that all buffers required in large quantities are prepared accurately, reproducibly, and traceably.

Additional automated biophysical characterization: Through the adjacent Rockefeller HTSRC facility, our laboratory also has access a GE/MicroCal Auto-iTC200 automated isothermal titration calorimeter (ITC) and a BioRad Proteon XPR36 surface plasmon resonance (SPR) instrument. Both instruments accommodate 96-well plates for fully automated runs, and are available for our use at low cost. Our laboratory automation platform will allow these experiments to be set up automatically.

Standard molecular biology equipment: The wet laboratory is also equipped for manual molecular biology.

Computational.

Local GPU cluster: The Chodera laboratory has priority access to a high-performance computing cluster with 1920 total hyperthreads and 120 NVIDIA GTX-680, GTX-TITAN, or GTX-TITAN-X GPUs. Project storage is provided by a high-performance shared 1.5PB GPFS storage system. Network connections are at least 1 Gbit/s throughout MSKCC facilities, and cluster, GPU, and storage systems are connected with 10 Gbit/s links. **Accounts on this cluster will be made available for all of our collaborators on this project to facilitate data interchange and access to adequate fast computational resources.**

GPU development resources: All Chodera laboratory members are equipped with laptop computers with GPUs capable of GPU-accelerated software development. All members also have access to five development GPU boxes contain an assortment of most available GPUs for development and automated software testing.

Folding@home: The Chodera laboratory is a participating laboratory in the Folding@home Consortium [<http://folding.stanford.edu>]. Folding@home is a distributed computing infrastructure run by Vijay Pande at Stanford University with over 350,000 actively computing cores, making it the most powerful distributed computing project in the world in terms of aggregate performance—19 PFLOP/s of aggregate computational power. The free availability of large quantities of computer time through this network—**which would otherwise cost tens of millions of dollars in hardware and power**—greatly leverages funding provided for this proposal. Access to the Folding@home network is provided via two dedicated servers at MSKCC connected to 180TB of usable storage in a high-availability datacenter.

EQUIPMENT – SEELIGER LABORATORY

Assigned to the Dr. Seeliger (PI) and located in newly-built laboratory:

1. Two thermal cycler (Eppendorf mastercycler ep) with temperature gradient and 96-well plate capabilities.
2. Refrigerated benchtop centrifuge (Eppendorf model 5810R) with rotor 15- and 50-mL conical tubes.
3. Spectrofluorometer (Horiba Jobin Fluoromax 4) with temperature controlled cuvette holder and polarizers for fluorescence anisotropy measurements.
4. Rapid mixing stopped flow system (Applied Photophysics RX2000) with temperature controlled chilling water bath.
5. Protein purification system (GE Biosciences AKTA Purifier UPC 10 FPLC) with UV absorbance detector, sample pump (P960) and fraction collector (Frac 950) in deli-case refrigerator.
6. Incubator shakers (2x New Brunswick Scientific I26R refrigerated, 1x Excella E24 for growing bacterial cultures).
7. Cell homogenizer (Avestin EmulsiFlex-C3) for bacteria and yeast cell lysis.
8. Ultralow freezer -80C (New Brunswick Scientific U570 with CO₂ backup system).
9. Superspeed centrifuge (Sorvall RC5b plus) with rotor (SS34) for protein purification.
10. Nikon SGZ1500 stereomicroscope with Nikon D5100 camera for crystal screening, documentation and crystal handling.

Core Equipment:

The equipment in the Center for Structural Biology, which has been described in the *Facilities and Other Resources* section, includes: two drop setting robots (Formulatrix NT8), dispensing robot (Formulatrix Formulatrix10), crystal plate hotel and automated microscope (Formulatrix RockImager), thermostated incubators, two Rigaku X-ray diffractometers (RU-H3R 18 kilowatt generator, MSC confocal blue mirror optics and a Raxis IV detector), fermentors, NMR instrumentation (8 instruments total ranging from 850 MHz and 2x 700 MHz to 300 MHz, cryogenic probes for 850MHz and 700MHz, cold probe for 500 MHz).

Equipment Shared With Other Investigators:

Dr. Seeliger and his group have unrestricted 24/7 access to the following shared equipment located in or adjacent to their lab space:

1. Refrigerated superspeed centrifuge (Sorvall Evolution) with rotors for 50-mL and 6x 1000-mL bottles.
2. Gel and immunoblot documentation systems (GE Typhoon FLA 9000, LI-COR Odyssey infrared imager; Bio-Rad Gel Doc).
3. Spectrophotometers (Thermofisher Nanodrop) with capabilities for measuring UV and visible absorbance in microliter droplets.
4. Absorbance plate reader (SpectraMax 340PC384) for spectral and kinetic measurements.
5. Isothermal titration calorimeter (Microcal VP-ITC).
6. Fluorescence plate reader (Victor 2, Perkin Elmer) with 96/384-well capabilities and fluorescence intensity and anisotropy detection modes.
7. SPR instrument (GE Biacore T-200) recently purchased with NIH award (1S10OD020155, PI Seeliger).
8. Dishwashers and autoclaves, scintillation counters, ultracentrifuges, confocal and fluorescent microscopes.

Equipment in the chemistry department (on-campus, 10 min walking distance) with unrestricted access:

1. Two CD instruments: An AVIV Model 202SF Stopped-flow circular dichroism spectrometer equipped with an automatic titrator and An Applied Photophysics Chirascan CD.
2. An Applied Photophysics Model SX18 stopped-flow fluorescence spectrometer
3. Beckman Coulter XL-I analytical ultracentrifuge

The pieces of major equipment described in this section, together with minor equipment described under Facilities & Other Resources, collectively constitute a biophysics-structural biology-biochemistry laboratory that has the full range of capabilities needed to complete the proposed project.

EQUIPMENT – GUNNER LABORATORY

Computation.

Our in-house cluster SYBIL has 192 cores. The resultant cluster will be adequate for MCCE jobs, which are very efficient. The home cluster has a 11.1 TB RAID storage for Gunner Lab archives.

We have access to a CCNY cluster with another 80 CPU nodes and 4 GPU compute nodes.

In the CUNY HPCC (High Performance Computing Center) system:

- Andy CPU cluster is an SGI cluster with 744 processor cores
- Penzias GPU cluster has 1,152 Intel Sandy Bridge cores each with 4 Gbytes of memory and supporting 136 NVIDIA Kepler K20 accelerators.